

Historic, archived document

Do not assume content reflects current scientific knowledge, policies, or practices.

Maine Agricultural Experiment Station

ORONO

BULLETIN 237

MARCH, 1915

The Assumption of Male Secondary Characters by a Cow With Cystic Degeneration of the Ovaries

CONTENTS.

	PAGE
Description of Case	66
Injection of Pituitary Body Substance	69
Post-Mortem Examination	72
Histological and Cytological Data	73
Discussion	76
Summary	79
Description of Figures	80

MAINE AGRICULTURAL EXPERIMENT STATION ORONO, MAINE.

THE STATION COUNCIL.

PRESIDENT ROBERT J. ALEY,	<i>President</i>
DIRECTOR CHARLES D. WOODS.	<i>Secretary</i>
CHARLES L. JONES, Corinna,	} <i>Committee of Board of Trustees</i>
FREELAND JONES, Bangor,	
WILLIAM A. MARTIN, Houlton,	
WILLIAM T. GUPTILL, Topsham,	
EUGENE H. LIBBY, Auburn,	
HOWARD L. KEYSER, Greene,	
FRANK S. ADAMS, Bowdoinham,	
LEONARD C. HOLSTON, Cornish,	<i>Commissioner of Agriculture</i>
	<i>State Grange</i>
	<i>State Pomological Society</i>
	<i>State Dairymen's Association</i>
	<i>Maine Livestock Breeders' Association</i>
WILLIAM G. HUNTON, Readfield,	<i>Maine Seed Improvement Association</i>

AND THE HEADS AND ASSOCIATES OF STATION DEPARTMENTS, AND THE
DEAN OF THE COLLEGE OF AGRICULTURE.

THE STATION STAFF.

<i>ADMINIS- TRATION</i>	{	CHARLES D. WOODS, Sc. D.,	<i>Director</i>
	{	BLANCHE F. POOLER,	<i>Clerk</i>
	{	GEM M. COOMBS,	<i>Stenographer</i>
	{	JANIE L. FAYLE.	<i>Stenographer</i>
<i>BIOLOGY</i>	{	RAYMOND PEARL, Ph. D.,	<i>Biologist</i>
	{	FRANK M. SURFACE, Ph. D.,	<i>Biologist</i>
	{	MAYNIE R. CURTIS, Ph. D.,	<i>Assistant</i>
	{	JACOB ZINN, Agr. D.,	<i>Assistant</i>
	{	JOHN W. GOWEN, B. S.,	<i>Assistant</i>
	{	JOHN RICE MINER, B. A.,	<i>Computer</i>
	{	HAZEL F. MARINER, B. A.,	<i>Clerk</i>
<i>CHEMISTRY</i>	{	JAMES M. BARTLETT, M. S.,	<i>Chemist</i>
	{	HERMAN H. HANSON, M. S.,	<i>Associate</i>
	{	EDWARD E. SAWYER, B. S.,	<i>Assistant</i>
	{	ELMER R. TOBEY, B. S.,	<i>Assistant</i>
	{	HOYT D. LUCAS, B. S.,	<i>Assistant</i>
	{	HARRY C. ALEXANDER,	<i>Laboratory Assistant</i>
<i>ENTOMOL- OGY</i>	{	EDITH M. PATCH, Ph. D.,	<i>Entomologist</i>
	{	ALICE W. AVERILL,	<i>Laboratory Assistant</i>
<i>PLANT PATHOLOGY</i>	{	WARNER J. MORSE, Ph. D.,	<i>Pathologist</i>
	{	MICHAEL SHAPOVALOV, M. S.,	<i>Assistant</i>
	{	VERNON FOLSOM,	<i>Laboratory Assistant</i>
<i>AROOSTOOK FARM</i>	{	GUY A. BAKER	<i>Superintendent</i>
<i>HIGHMOOR FARM</i>	{	WELLINGTON SINCLAIR,	<i>Superintendent</i>
ROYDEN L. HAMMOND,		<i>Seed Analyst and Photographer</i>	
CHARLES C. INMAN,		<i>Assistant</i>	

BULLETIN 237.

SEX STUDIES. VII. ON THE ASSUMPTION OF MALE SECONDARY CHARACTERS BY A COW WITH CYSTIC DEGENERATION OF THE OVARIES.¹

RAYMOND PEARL AND FRANK M. SURFACE.

Evidence regarding the relation between somatic secondary sexual characters and the primary sex organs, the gonads, is derived in the main from one or another of three sources, viz.:

1. Castration experiments.
2. Transplantation, or organ extract injection experiments.

¹Papers from the Biological Laboratory of the Maine Agricultural Experiment Station, No. 82.

This paper forms the seventh in a series of studies on various phases of the problems of sex determination and secondary sexual characters which have been published by the senior author and his associates during the past seven years. In accordance with a general policy of the laboratory it is proposed that, in the future, papers dealing with these problems shall appear under the general title "Sex Studies." The papers which have already appeared in this series, and which are now assigned numbers in the order of their appearance, in accordance with the above mentioned policy, are:

Sex Studies I. On the Relation of Race Crossing to the Sex Ratio. By Maud Dewitt Pearl and R. Pearl. Biol. Bul., Vol. XV, pp. 194-205, 1908.

II. A Case of Hypospadias in a Ram. By R. Pearl. American Vet. Rev., Vol. XL, No. 6, pp. 794-796, 1912.

III. The Interstitial Cells and Supposed Internal Secretion of the Chicken Testis. By A. M. Boring, Biol. Bul., Vol. XXIII, pp. 141-153, 1912.

IV. Fat Deposition in the Testis of the Domestic Fowl. By R. Pearl and A. M. Boring, Science, N. S., Vol. XXXVI, pp. 833-835, 1912.

V. Data on Sex Determination in Cattle. By R. Pearl and H. M. Parshley. Biol. Bul., Vol. XXIV, pp. 205-225, 1913.

VI. The Relative Time of Fertilization of the Ovum and the Sex Ratio Amongst Jews. By R. Pearl and Redcliffe N. Salaman. Amer. Anthropol., Vol. XV (N. S.), pp. 668-674, 1914.

3. Pathological and teratological cases (including hermaproditism) in which some lesion or developmental abnormality of the gonads is accompanied by a change in the secondary characters.

The present paper is offered as a contribution to the data on this problem under the last category.

DESCRIPTION OF CASE.

A pure-bred registered Ayrshire cow, Dorothy of Orono (23010), bred and owned throughout her life by the University of Maine, had the following history. Her sire was Roderick Dhu (8590) and her dam Dorothy Alaska (14012), a cow showing no sexual abnormality or derangement of any kind. Dorothy of Orono was dropped October 19, 1906.

She proved a regular breeder in the earlier years of her adult life, as is shown by the following table.

TABLE I.

Breeding Record of Dorothy of Orono.

Date of Birth of Calf.	Sex of calf.	NOTES ON OFFSPRING.
1909, Sept. 17	♂	Cross-bred calf sold as skinner.
1910, Sept. 10	♀	Pure-bred Ayrshire heifer Dot Alaska (29353). Still owned by University of Maine. Has never shown any sex abnormalities.
1912, Feb. 24	♂	Cross-bred calf, sold as skinner

When 3 years and 327 days old Dorothy of Orono was started on an official milk test of one year, which she completed with a record of 11463 lbs. of milk, carrying 417.71 lbs. of butter fat. For this record she was entered as No. 426 in the Ayrshire Advanced Registry.

Her complete lactation record is shown in Table 2.

TABLE 2.

Lactation Record of Dorothy of Orono.

LACTATION PERIODS.	Days in milk.	Pounds of milk.	Pounds of fat.	Remarks.
Sept. 21, 1909-Aug. 4, 1910.....	316	7,840.6	293.62	Lactation in which Advanced Registry record was made.
Sept. 11, 1910-Nov. 25, 1911.....	440	12,426.4	450.75	
Feb. 26, 1912-March 24, 1913.....	391	7,016.8	253.92	Cow was sick for sometime during this period.

At this point begins the interesting part of the history. After March 24, 1913, the cow never gave any milk. The udder rapidly shrunk to a very small size and the animal began to show the external characteristics of a bull. This change was very slight at first but soon became much more marked. *After a lapse of 8 months the general external facies and the behavior of the cow were like those of a bull to a remarkable degree.* The neck had become thickened in its posterior parts, and had developed a well marked crest, as is characteristic of a bull. If the cow had been so screened that only her fore-quarters and neck were visible any observer would have unquestionably pronounced her a male. The assumption of male characters in these regions was complete and perfect. In the hind-quarters the change from characteristic female conformation in the male direction, while less striking than in the anterior parts, was still clearly evident. The udder shrunk away to a very small size. The hips and rump took on the smooth, rounded, filled-out appearance which is characteristic of the bull but not of the cow.

Altogether the assumption of male secondary characters was so distinct as to arrest at once the attention of all who saw her in the barn, including casual visitors who knew nothing of the history of the animal. It is extremely difficult to describe the change exactly, chiefly because the secondary sexual characters in cattle are so indefinite. Anyone acquainted with cattle can tell at a glance the sex of a mature animal from its general bodily conformation, without looking at the sex organs, but it is difficult to itemize the differences. Perhaps the crest in the male, and the associated development of hair on the dorsum

of the neck and head is the most striking male secondary character. This character was very completely developed by the cow Dorothy of Orono. Unfortunately, owing to a misunderstanding, we have no photographs of the animal, showing the condition before and after the change.

The change in behavior of the animal was as striking as that in conformation, though not so easy of interpretation. Before considering this, it should first be noted that after the cow dropped her third calf on February 24, 1912, she was put to the bull and received service on the following dates, all in 1912: May 30, June 23, July 15, August 13, October 15, October 30, and November 16. On each of these occasions she showed some evidence of oestrus, but on the later dates in the series the manifestations were slight, and an increasing disinclination to take the bull became evident. After November 16, 1912, she never came again in heat up to the time she was killed (February 19, 1914), nor would she receive the bull.

During this time she showed the sex behavior of a bull, attempting copulation with the cows. At first this behavior was discriminatory, only those cows which were in heat being mounted. In fact this cow Dorothy of Orono was during this time used by the herdsman to test other cows for the presence of oestrus. Later all discrimination was lost and she would mount any cow within reach.

At no time did she show characteristic symptoms of nymphomania, unless the mounting of other cows be so interpreted. Such behavior ("bulling") is, to be sure, one of the manifestations of oestrus in many normal cows, and is sometimes observed in nymphomania.² Hess (quoted in Williams, *loc. cit.*, p. 174) says on this point: "In some cases of nymphomania, the affected animals attempt to mount neighboring cows, bulls, oxen, and even persons and continue to ride the former for a long interval; on the other hand they permit bulls and also other cows to mount them constantly." The difference between the latter type of behavior and the case here described is evident. Hess however says, farther on, that cases of nymphomania associated with cystic ovaries do occur, in which the individuals refuse to receive the bull, or to be mounted by other cows.

²Cf. Williams, W. L. Veterinary Obstetrics. Ithaca, 1900.

The whole question of the correct interpretation of abnormalities of sex behavior in cattle is a difficult one. There is a lack of precise information collected by competent behaviorists either in regard to the normal or the abnormal behavior. It is not at all impossible that all of the behavior which has been called nymphomania in cattle is really not the equivalent of the behavior so designated in women, but is rather an assumption, in greater or less degree, of the male sex behavior.

In any case great caution must be used in drawing conclusions regarding the relation between secondary sexual characters and primary sex organs from behavior data. Such data probably have but little, if any, critical value in this connection, because of the facts: (1) That the vicarious assumption in greater or less degree of the copulatory behavior of the other sex is of wide-spread and fairly frequent occurrence among higher vertebrates, particularly the domestic animals. (2) That such *changes* of behavior are as likely to be associated with an increased physiological tonus or activity of the gonads as with a decreased tonus or activity. Much current discussion of the problem of secondary sexual characters is extremely uncritical, in that it overlooks or disregards completely these facts, which are well known to students of the comparative psychology of sex and to those who, from long experience, are intimately familiar with the behavior of higher animals.

In the present case we are inclined to the view that the cow's sex behavior really changed to that of a male, coincidentally with the physical changes already described. We would not, however, lay much stress upon the point for the reasons above indicated.

INJECTION OF PITUITARY BODY (ANTERIOR LOBE) SUBSTANCE.

Before this cow was killed for autopsy it was thought desirable to determine whether by treatment of the animal with the substance of some endocrinal gland it might be possible to bring about a change in its sex behavior or in the external sex characters (udder, etc.). After careful consideration of the matter it was decided to try in this connection the substance of the anterior lobe of the pituitary body. The reason for this choice was the known connection between the pituitary body and the

genital system. On this point Swale Vincent² says (*loc. cit.* p. 403): "A relation between pituitary and ovary is shown by the fact.....that in castrated women and animals there is frequently enlargement of the pituitary. Further after destructive diseases of the reproductive glands the pituitary reacts by hypertrophying." Also (p. 402) the same author calls attention to the fact that: "The pituitary during pregnancy resembles an epithelial tumor. The increase in amount of secretion is seen by the fact that one can squeeze a milky juice out of the gland. The hypertrophy persists to a certain degree, even after pregnancy, so that the weight of the gland in a multipara may be three times as great as that of a normal gland." Aschner³ summarizes the more important results of his very thorough study of the physiology of the pituitary gland, so far as concerns the female genital organs in the following words (*loc. cit.* pp. 88 and 89).

"Hier finden sich bei erwachsenen Hunden leichte Degenerationserscheinungen an den Ovarialfollikeln und Abnahme des Fettes der interstitiellen Drüse in den ersten Wochen nach der Hypophysenexstirpation. Am Uterus sind kaum wesentliche Veränderungen nachweisbar, auch nicht im Sinne der Kastrations-atrophie. Das Auftreten der Brunst wird bei erwachsenen Tieren zwar nicht ganz gehemmt, aber doch deutlich abgeschwächt. Eine Gravidität kommt dabei niemals zustande. Eine bestehende Gravidität wird durch Hypophysenexstirpation unterbrochen.

"Bei jugendlichen Weibchen sind die Genitalveränderungen wieder sehr auffallende.

"Nach Exstirpation der Hypophyse in den ersten 3 Lebensmonaten zeigt sich ungefähr innerhalb der ersten 6 Wochen eine starke Abnahme der interstitiellen Drüse, fast bis zum Schwund derselben. Die Entwicklung der Ureier zu Follikeln wird bei den operierten Tieren um vieles verzögert, auch bleiben die Follikeln stets auffallend spärlicher als bei normalen Tieren.

²Vincent, S. *Internal Secretion and the Ductless Glands*. London. 1912. An extensive bibliography is given in this work and it is not thought necessary here to cite earlier authorities in detail, since they can be found in Vincent's book.

³Aschner, B. Ueber die Funktion der Hypophyse, *Pflüger's Arch.* Bd. 146, pp. 1-146, 1912.

Eine vollständige Gleichwertigkeit der Keimdrüsen mit denen der normalen Tiere wird nie, auch nach vielen Monaten nicht erreicht.

“Alle diese trophischen Störungen werden in gleicher Weise durch die Exstirpation der ganzen Hypophyse ebenso wie durch die Exstirpation des Vorderlappens allein hervorgerufen.

“Der Hinterlappen der Hypophyse ruft diese Erscheinungen bei seinem Ausfall nicht hervor.”

Goetsch and Cushing⁵ have lately shown that the feeding of the dessicated extract of the anterior lobe of the hypophysis to young rats of both sexes “has a markedly stimulating effect upon the growth and development of the reproductive glands.” This was evidenced both by the histological condition of the sex glands and the early and frequent breeding of the treated animals. Posterior lobe extract has no such effect.

Adler⁶ has shown that in *Rana temporaria* and *Pelobates* larvae, hypophysectomy inhibits the development of the sex glands.

It seemed highly desirable, in view of the above mentioned results, to determine what effect the continued injection of anterior lobe substance would have in the case of this cow Dorothy of Orono, whose sexual functions were deranged in the manner already indicated.

As material for these experiments we used the dessicated powdered substance of the anterior lobe of the pituitary glands of cows. This material we obtained from the Organotherapeutic Department of Armour & Company in Chicago. The protocols of the experiment follow:

November 25. Injected 1-2 gram of dessicated pituitary body anterior lobe mixed with 18 cc. 0.9 per cent. NaCl solution into the jugular vein at 10.30 A. M. No ill effects observed. Temperatures (Fahrenheit and rectal in all cases)—12 M., 101.4; 3 P. M., 101.8; 5 P. M., 101.8; morning of November 26, 101.4. (This was the second

⁵Goetsch, E. and Cushing, H. The pars anterior and its relation to the reproductive glands. Proc. Soc. Exp. Biol. and Med., Vol. XI, pp. 26-27, 1913.

⁶Adler, L. Metamorphosenstudien an Batrachierlarven. I. Extirpation endokriner Drüsen. Arch. f. Entwickl., Bd. 39, pp. 21-45, 1914.

injection but in the first the syringe did not work well and only a few cc. were given).

December 1. Injected 1-2 gram of same powder mixed with 10 cc. of 0.9 per cent. NaCl solution at 10.30 A. M. Temperatures:—11 A. M., 102.0; 1.30 P. M., 101.2; 3.40 P. M., 101.0; 5.30 P. M., 100.4; December 2, 8.30 A. M., 101.6.

December 5. Injected 1-2 gram of same powder in 15 cc. NaCl solution subcutaneously at 11.15 A. M. Cow seemed to show some rumbling or difficulty in breathing when we came to inject her. For this reason we used subcutaneous route. Temperature just before injection. 11.15 A. M., 102.1; 12 N., 102.5; 2 P. M., 102.1; 5 P. M., 102.1.

December 9. Injected same dose subcutaneously at 11.30 A. M.

December 10. Same dose subcutaneously at 11.15 A. M.

December 11. Same dose intravenously at 10.20 A. M.

December 15. Injected 3-4 gram powder in 18 cc. 0.9 per cent. NaCl solution subcutaneously at 10.30 A. M.

December 16. Injected 3-4 gram in 22 cc. 0.9 per cent. NaCl solution; about half injected intravenously and half subcutaneously.

At this point the injections were stopped since the results had been absolutely negative so far as concerned the sexual functions of the cow. Of course the period included was too short for any structural changes in secondary sexual characters to have appeared. On the other hand, it was a sufficiently long period for any effect on the abnormal sex-behavior, the udder, or the external genitals to have appeared. There was not the slightest change in any of these respects, either during or after the period of the injections.

POST-MORTEM EXAMINATION.

On February 18, 1914, the cow was slaughtered. She was in good flesh and all the viscera were normal with the exception of the genital organs. The ovaries both showed extensive

cystic degeneration (cf. figs. 4A and 4B). The whole ovary in each case was a mass of cysts of varying sizes. The walls of the cysts were made up of fibrous connective tissue and were very tough and resistant to rupture. The uterus and tubes were very small, practically in infantile condition. The ovaries, slit open to show the cysts, together with the ovaries of a normal cow are shown in figs. 3 and 4. The cystic ovaries showed no corpora lutea recognizable as such. The case is clearly one of multiple cystic degeneration of the ovaries.

HISTOLOGICAL AND CYTOLOGICAL DATA.

At the time of autopsy the ovaries of this cow were split in halves longitudinally and immediately fixed in McClendon's¹ fluid. At the same time the ovaries from a normal cow of about the same age as the one here under discussion were removed and fixed in the same fluid for comparison. Subsequently this material was sectioned by Dr. Maynie R. Curtis and stained in various ways.

The outcome of the study of this material is interesting from several standpoints, but particularly so in relation to the problem of secondary sex characters and the gonads. For it appears, after very careful study of the material, that *histologically and cytologically these cystic ovaries differ from the normal cow ovary in but one essential respect, namely that they have not corpora lutea*. The absence of luteal substance arises from the fact that ovulation does not occur. The oöcytes start their development in a perfectly normal way in the cystic ovary (figs. 5, 9, and 10). But after the follicle has reached the size at which it normally breaks and discharges its ovum, it still keeps on growing in the cystic ovary. Either through some physiological abnormality in the follicular epithelium which affects its secretory powers, or through some change in the permeability of the follicular walls, it results that the liquor folliculi keeps increasing in amount and the follicle does not rupture. Since no ovum is discharged, no corpus luteum can be

¹McClendon, J. F. Preparation of Material for Histology and Embryology, etc. Anat. Rec. Vol. VII, pp. 51-61, 1912.

formed. The study of this case leads to exactly the same conclusions regarding ovarian physiology as those of Meyer⁸.

Specifically the findings are as follows. The surface or germinal epithelium of the ovary is entirely normal, and agrees with the description and figures of Schmaltz⁹ (*loc. cit.*) This is shown in fig. 5. Under this is seen the fibrous connective tissue layer, poor in cells, as in the normal cow ovary (the Schleimhautkörper of Schmaltz). Beneath this is the zona follicularis, with as many, and entirely similar follicles, as the normal ovary. A young oöcyte in which there has been no proliferation of follicle cells, or formation of liquor folliculi is shown in fig. 10. Fig. 9 shows an older oöcyte, in which the liquor folliculi is forming. These are entirely normal.

Interstitial cells in equal number, and with precisely the same cytological characteristics as in the normal ovary, are found in this cystic ovary. Two of these cells in one field of a 1-12 immersion objective are shown in fig. 6. As there is no detailed description of the interstitial cells of the cow's ovary in the literature, and as the technique we have used differentiates these cells with extraordinary clearness it seems desirable to describe them with some particularity. This description is equally applicable to the interstitial cells of the cystic ovary and those of a normal ovary, since these cells are absolutely indistinguishable in the two cases.

The interstitial cells are larger than the surrounding connective tissue cells of the ovarian stroma. Their outline, which is always clean-cut and definite, varies with the degree of crowding to which they are subjected from neighboring cells. They are usually rounded in outline but may be considerably elongated in one direction, leading to something approaching a spindle shape. Their large size, as compared with the non-secreting stroma cells, is due almost entirely to the size of the cell body and not to the nucleus. The nuclei of the interstitial cells are of the same order of magnitude as those of the surrounding connective tissue cells. These interstitial cells are found in all

⁸Meyer, R. Ueber die Beziehung der Eizelle und das befruchteten Eies zum Follikelapparat, sowie des Corpus luteum zur Menstruation. Arch. f. Gynaek., Bd. 100, pp. 1-19, 1913.

⁹Schmaltz, R. Die Struktur der Geschlechtsorgane der Haussäugetiere mit anatomischen Bemerkungen. Berlin (Parey), 1911.

parts of the ovary, but more numerous in the neighborhood of follicles and blood vessels. A study of free-hand sections stained with Sulan III, as used by Schaeffer¹⁰ in her comparative studies on the secretory interstitial tissue of the ovary, shows precisely the same general distribution of this tissue in the normal and the cystic ovary.

The most striking thing about the interstitial cells, when they are properly differentiated by the stain, is the mass of granules of secretion which they contain (cf. figs. 6, 7, and 8). Some of the cells are so loaded with these granules that nothing else can be seen. The nucleus is completely covered. From this condition every gradation may be found to the other extreme when the cell is entirely empty of secretion granules.

For the precise definition of these cells we have found nothing equal to Kresylechtviolett¹¹, following the formalin fixation of McClendon's fluid. The stain should be differentiated in alcohol, to a point where the nuclei have nearly lost all contrast, and have practically the same pale blue as the cytoplasm of the connective tissue cells. Then it will be found that the granules of secretion in the interstitial cells are stained sharply and intensely purple. The contrast, when the staining is properly done, between the ordinary connective tissue and other cells of the stroma, and the interstitial cells with their granules of secretion, is extreme.

Returning to the general consideration of the histology of the cystic ovaries in this case, it may be pointed out that, while, after the pathological condition intervened, evidently any follicles which got well started on the road to development went on and formed cysts, yet in the body of the ovary are to be found the characteristic remains of earlier follicles, just as in a normal ovary. One of these old atretic follicles is shown in fig. 5 at *x*.

¹⁰Schaeffer, A. Vergleichend histologische Untersuchungen über die interstitielle Eierstocksdrüse. Arch. f. Gynaek., Bd. XCIV, pp. 491-541, 1911. 2 Pl.

¹¹Morse, R. L. Kresylechtviolett. Jour. Appl. Micros., Vol. 4, pp. 1492-1494, 1901.

DISCUSSION.

The case described in the preceding pages presents for consideration certain definite and clear-cut results bearing on the problem of secondary sex characters. These are:

1. This cow had been a perfectly normal female and had performed all the reproductive functions, both primary and secondary, of that sex.

2. It later assumed certain of the secondary characters of the male, both in respect of structure and behavior, with perfect definiteness, and, so far as the characters concerned go, completeness. This change was, for example, at least as complete and definite as any of those described by Steinach²² following castration and transplantation of gonads.

3. The gonads of this animal, examined subsequent to the change in secondary characters, were exactly like those of a normal cow, save in the one respect that the follicles were not breaking and discharging ova, but were forming follicular cysts or becoming atretic, and because of this no corpora lutea were formed.

a. The interstitial secreting mechanism of these ovaries was absolutely normal, both in respect of number of cells, and the cytological characteristics of the individual cells.

b. The germinal mechanism was perfectly normal up to the point where ovulation should occur. Then it failed to separate the ova from the ovary.

c. The outstanding, and so far as we can determine the only significant, anatomical and physiological difference between the gonads of this abnormal cow and those of a normal one, consists in the fact that the former lacked any luteal tissue.

From the above facts it appears clear at once that in this case the change in the secondary sex characters cannot with any degree of plausibility be attributed to any activity (or failure of activity) of the interstitial cells. On the other hand, the suggestion is evident that the change is associated with

²²Steinach, E. Willkürlich Umwandlung von Säugetiermännchen in Tiere mit ausgeprägt weiblichen Geschlechtscharakteren und weiblicher Psyche. Pflüger's Arch., Bd. 144, pp. 71-108, 1912.

the absence of luteal tissue. This cow probably ovulated for the last time about November 16, 1912 (see page 69 *supra*). At least she ceased at that time to show signs of oestrus, which in the cow are associated with ovulation. By the following summer, supposing ovulation to have stopped at the date suggested, luteal tissue in the ovary would either have entirely disappeared or been reduced to a very small amount. But it was at this time (summer of 1913) that the cow began visibly to take on the secondary characters of the male. On the whole, the evidence seems as complete as it is possible to make it from observational data (in the absence of experimental) that the absence of luteal substance in the ovaries was causally connected with the assumption of male secondary characters. It is greatly to be regretted that this cow was not injected with corpus luteum instead of pituitary body substance.

The view above outlined suggests that the corpus luteum is one of the chief active ovarian agents in mammals in maintaining the "femaleness" of the individual, in addition to its other functions of inhibiting ovulation, etc. There is a good deal of evidence that such is in fact the case.

One line of evidence of this sort is furnished by the clinical data following administration of corpus luteum material in one form or another in cases of arrested sexual development in the female. It is not the place here to review this literature in detail. One very clear-cut and definite case may be cited, however. This case, from the standpoint of the biologist, is particularly favorable and pertinent in the present connection, since it is free from any associated pathological disturbances which so frequently make the interpretation, from a theoretical standpoint, of clinical data very difficult or impossible.

The case referred to is one reported by Elliott¹³. The essential facts are as follows: I have italicized the parts of particular interest from the present standpoint.

"Patient. Mrs. M., white, aged 27, married *five* years, has never been pregnant, and is anxious to have a child.

"Examination. General condition good, muscular, not fat; *figure* like that of a boy of 18; narrow hips, undeveloped

¹³Elliott, H. R. A Case of Infantile Uterus and Appendages with Result of Treatment. Jour. Amer. Med. Assoc., Vol. LXII, pp. 1085-1086, 1914.

breasts. Heart and lungs normal. *Uterus* about size of English walnut, *ovaries*, not palpable. (Has been examined by gynecologist who told her she could never have a child). Pelvis normal. Has had *menstrual* show of a few drops three or four times during her life. Epistaxis very free at times. *Sexual* feeling very slight, if at all, and only very seldom. Several members of family have had menstrual disorders, but none of this type.

"Treatment and Result. April 6, 1912: Patient was put on extract of luteum tablets, one three times daily for a week, two three times daily for another week, then returning to the first dosage. Some uterine massage was given."

"On May 20, 1912, menses appeared for a day. Patient had sensation of approaching menses in June, but only a pink show. She had a mild epistaxis. General condition is good: she seems to be rounding out. Becoming discouraged, patient abandoned treatment.

"Extract of luteum treatment was advised and started again in September, 1912. Uterus seems larger and cervix longer than in June. Last part of October patient had slight menstrual show, first time since June.

"Nov. 3, 1912: Patient noticed more sexual feeling last month.

"Nov. 25, 1912: No menses since show in October. Patient very much stouter, breasts enlarged, uterus larger, cervix longer. *Pregnancy* suspected and cautions given.

"Jan. 24, 1913: *Uterus* much larger, size of large pear, cervix long and firm. *Breasts* much larger, hips larger: general appearance of woman's *figure* instead of boy's. Side view, prominent above pubes, as in three and a half to four months' pregnancy."

At 6 P. M. on July 2, 1913, the patient was delivered normally of a male child.

In this case we have at the outstart an infantile condition of the uterus and essentially an indifferent condition of the secondary sex characters. Following the luteal medication there was a marked change to the distinctively female condition.

The data presented in this paper support very clearly the conclusion which has been reached by Below¹⁴, Frank¹⁵ and others, that there is a sharp distinction between the secretions of corpus luteum and interstitial cells in respect of their effect upon the organism. That the interstitial cells had nothing to do with the secondary sex characters in this case seems entirely clear.

SUMMARY.

This paper describes the reproductive history of a cow, which presents the following points of interest:

1. The cow was initially a perfect female, bearing calves and making a very high milk record.

2. Later she failed to come in heat, and gradually, but in the end to a very marked degree, took on male secondary sex characteristics, both in behavior and structure.

3. The gonads of this animal, examined subsequent to the change in secondary characters, were exactly like those of a normal cow, save in the one respect that the follicles were not breaking and discharging ova, but were forming follicular cysts, or becoming atretic, and because of this no corpora lutea were formed. The interstitial secreting mechanism of these ovaries was absolutely normal, both in respect of number of cells, and the cytological characteristics of the individual cells.

4. The evidence from this case strongly suggests that one function of the corpus luteum, through its internal secretion, is to maintain in full development the female secondary sex characters.

5. Repeated injections of a suspension of the dessicated substance of the anterior lobe of the pituitary body failed to bring about any change in the sex behavior of this cow after it had assumed a male character.

¹⁴Below, N. A. *Glandula lutea und Ovarium in ihrem Verhalten zu den normalen physiologischen und pathologischen Vorgängen im weiblichen Organismus.* Monatschr. f. Geburtsh. u. Gynaek., Bd. XXXVI, pp. 679-696, 1912.

¹⁵Frank, R. T. *The Functions of the Ovary*, Surg., Gynaec., and Obst., Vol. XIII, pp. 3-53, 1911.

DESCRIPTION OF FIGURES.

Figs. 3A and 3B. Photographs of normal ovaries of a healthy cow about 6 years old. Note in fig. 3A the large freshly formed corpus luteum on the right. A smaller, involuting corpus luteum is seen at the same level to the left in fig. 3A. In both figs. 3A and B very small, far-regressed corpora lutea can be seen scattered at various points on the ovary. (Slightly reduced below natural size).

Figs. 4A and 4B. Photographs of cystic ovaries of the cow Dorothy of Orono. In both cases the ovary has been slit longitudinally and opened out in order to show the size and distribution of the cysts. No corpora lutea are visible nor were any to be seen on any part of these ovaries. (Relative reduction as in Figs. 3A and B).

Fig. 5. Low power photomicrograph of a section through one of the cystic ovaries of Dorothy of Orono. This shows at the top a normal germinal epithelium and below it the fibrous connective tissue layer (Schleimhautkörper); below this is the zona follicularis showing numerous follicles in various stages of development. At the left at the level indicated by *x* is seen an old atretic follicle scar of entirely normal appearance ($\times 35$).

Fig. 6. Photomicrograph of a section of cystic ovary showing normal interstitial cells loaded with secretion at *a*. ($\times 710$).

Fig. 7. Camera lucida drawing of a normal interstitial cell from the cystic ovary. This figure shows the large, plump cell body and distinct outline. Granules of secretion are scattered through the cytoplasm. This cell contains relatively few of these granules of secretion, and is to be contrasted in this particular with cells like those shown in Fig. 6 or Fig. 8. ($\times 2835$).

Fig. 8. Camera lucida drawing of a normal interstitial cell from a cystic ovary. This cell shows in comparison with Fig. 7, the elongated, somewhat spindle-shape of the cell body due to pressure of surrounding cells, and the extreme condition of loading of the cell-body with granules of secretion. The lighter area in the lower part of the cell indicates the position of the nucleus, the outline of which, however, cannot be seen because of the secretion granules. ($\times 2835$).

Fig. 9. Photomicrograph of a normal Graafian follicle from cystic ovary. This follicle is quite far advanced in its development, the liquor folliculi already filling nearly a half of the follicle. ($\times 89$).

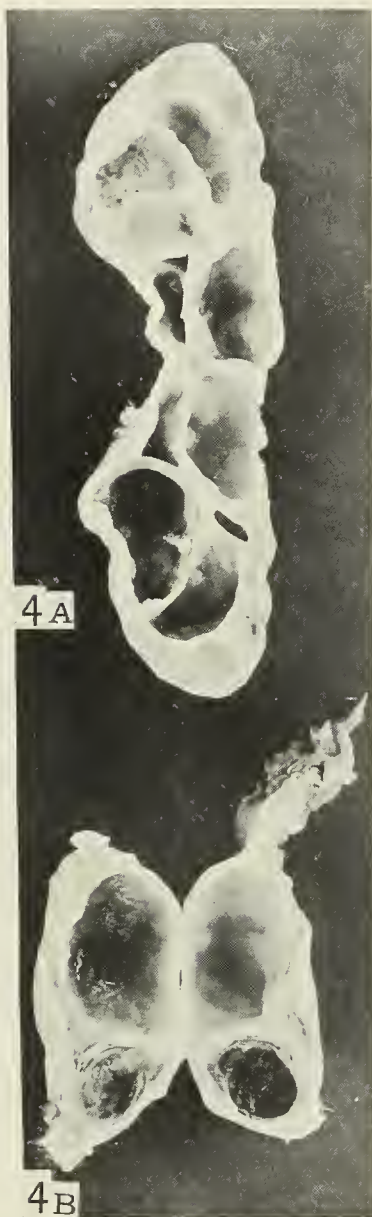
Fig. 10. Photomicrograph showing a normal very young Graafian follicle from cystic ovary. In this case the cell body of the primitive oöcyte completely fills the Graafian follicle. There has been no formation of liquor folliculi, nor proliferation of the follicular epithelial cells. A single row of nuclei of these follicular cells may be seen surrounding the oöcyte. ($\times 710$).



3A



3



4A

4B



